



Case Report

Erythema nodosum leprosum: A rare cause of testicular nodules

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ABSTRACT

Erythema nodosum leprosum (ENL), characterized by erythematous subcutaneous nodules with multiorgan involvement and systemic manifestations such as neuritis, arthritis, and orchitis, affects approximately 50 % of patients with lepromatous leprosy (LL). It has also been associated with testicular atrophy and adult-onset hypogonadism, but testicular nodules have rarely been reported. We present the case of a 35-year-old male patient with biopsy confirmed LL who completed multidrug therapy and presented for follow-up with a complaint of testicular tenderness. His disease course had been complicated by ENL and polyneuritis. At the time, physical examination revealed a palpable tender nodule in the left testicle. Testicular ultrasound and magnetic resonance imaging showed bilateral intratesticular masses, of which the differential diagnosis included malignancy and inflammatory or postinfectious granulomatous process. Laboratory workup, testicular malignancy markers, and hormone levels were within normal limits. In view of the patient's underlying condition and after Urology evaluation, a diagnosis of granulomatous process was favored. The patient completed a prednisone taper followed by a 3-day prednisone pulse and weekly methotrexate, with sequential testicular ultrasounds to monitor response. After a year of close follow-up and slow tapering of methotrexate, the patient achieved complete resolution of the left intratesticular mass and decrease in size of the contralateral mass, evidenced by both physical examination and imaging. This case highlights the importance of a high index of suspicion in patients with LL and ENL who present with testicular nodules, as awareness of testicular involvement in this population is imperative to avoid life altering procedures such as orchiectomy.

Introduction

Leprosy or Hansen's disease (HD) is a chronic granulomatous infection caused by *Mycobacteria lepra* complex (MLC), comprised of *Mycobacterium leprae* and *Mycobacterium lepromatosis*, affecting primarily the skin and the peripheral nervous system. Host immunological response determines the clinical presentation as described by Ridley Joplings leprosy spectrum [1]. *Mycobacterium leprae* may disseminate via the lymphatic or vascular systems or by direct invasion causing multisystemic disease especially in the lepromatous border [2]. Testicular involvement is reported frequently most probably due to the favorable growth of MLC in areas of lower body temperature such as the testis. Erythema Nodosum Leprosus (ENL) is one of the immune mediated reactions that arises as a complication of HD and affects approximately 50 % of the patients in the lepromatous border [3]. ENL can develop before, during or after multibacillary multi-drug therapy

(MB-MDT) for leprosy and can recur for several years [4]. Involvement of ENL has been reported in several organs including the testes, where it usually presents as generalized testicular tenderness [5]. This case reports a rare clinical presentation of ENL as a testicular nodule in a patient previously diagnosed with lepromatous leprosy (LL) and relapsing-remitting ENL.

Case presentation

We present the case of a 35-year-old male patient with confirmed LL since 2013 who completed 24 months of multidrug therapy with daily rifampin 600 mg, dapsone 100 mg, and clofazimine 50 mg. His disease course had been complicated by recurrent ENL treated with prednisone since 2015. In 2016, having completed MDT and still on prednisone for ENL, the patient was started on methotrexate (MTX) 15 mg as a steroid-sparing agent. One year later, the patient was successfully tapered off

Abbreviations: ENL, erythema nodosum leprosum; HD, Hansen's disease; LL, lepromatous leprosy; MB-MDT, multibacillary multi-drug therapy; MLC, *Mycobacteria lepra* complex; MTX, methotrexate.

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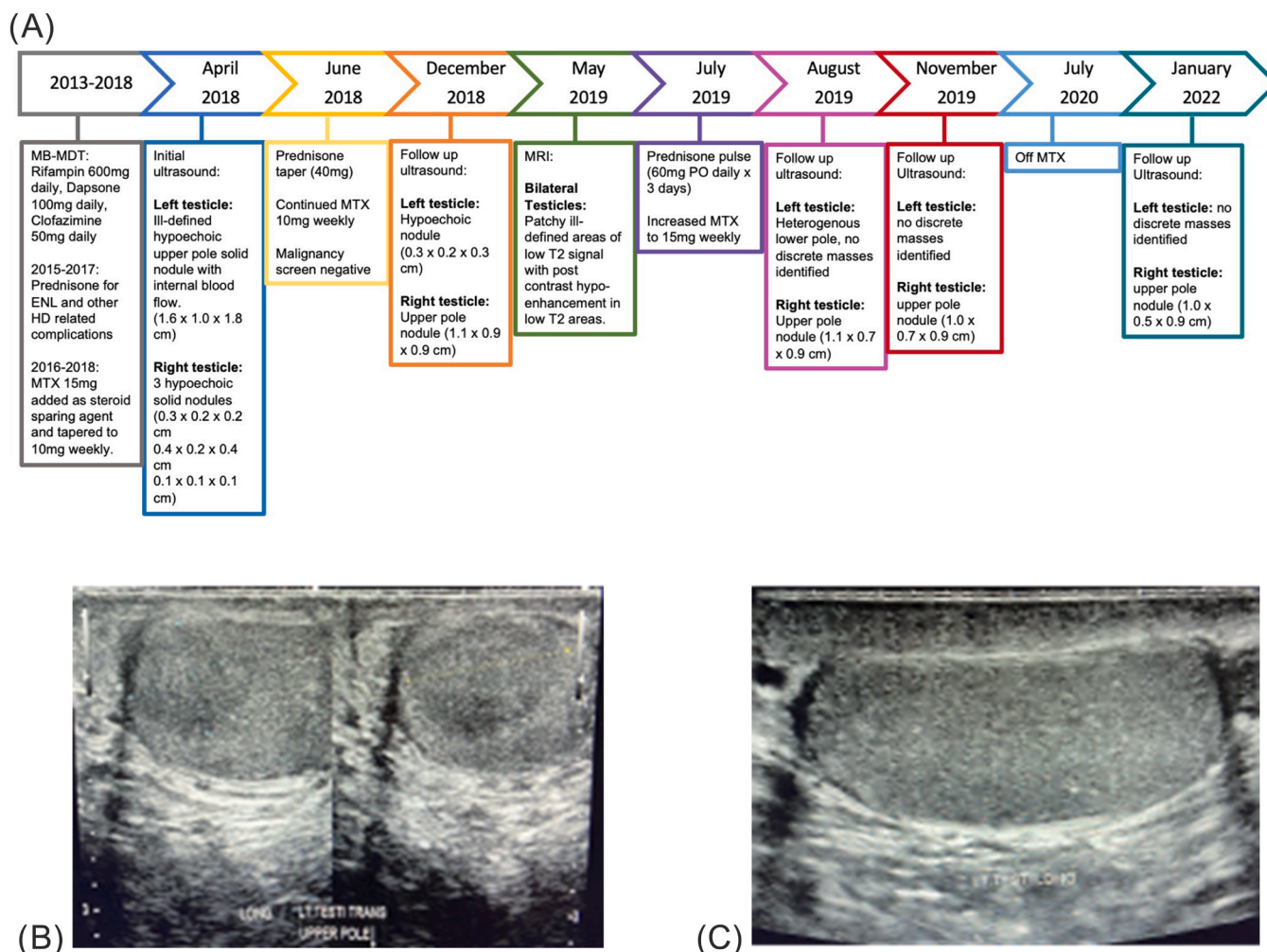


Fig. 1. Patient management and imaging. (A) Patient treatment timeline. (B) Ultrasound of left testicle nodule on April 2018. (C) Ultrasound of left testicle nodule on January 2022.

prednisone and continued MTX 10 mg weekly with improvement of ENL. At the time, the patient was unable to further decrease MTX due to the appearance of new ENL lesions. In April 2018, the patient presented with left testicular tenderness and physical examination revealed a palpable tender nodule in the left testicle for which urology evaluation and tests were ordered. In June 2018, the patient also developed polyneuritis and Tarsal tunnel syndrome. The testicular ultrasound and magnetic resonance imaging showed bilateral intratesticular masses, for which the differential diagnosis included malignancy and an inflammatory or post-infectious granulomatous process. Testicular malignancy workup including beta-human chorionic gonadotropin, alpha-fetoprotein, and lactate dehydrogenase were within normal limits. After the case was discussed with the Urologist and the Medical Director of the National Hansen Disease Program, and in view of clinical picture, patient history, negative lab results for malignancy, and MRI results suggestive of a granulomatous process, the diagnosis of ENL was favored. Therefore, in June 2018, the patient received a 40 mg prednisone taper and MTX was continued at 10 mg weekly for management of both his ENL and other HD complications. In July 2019, the left testicular nodule had started to decrease in size, and he was then given a three-day 60 mg prednisone pulse along with weekly MTX 15 mg. After a year of close follow up, the patient achieved complete resolution of the left intratesticular mass and minimal decrease in size of the contralateral mass, evidenced by both physical examination and sequential ultrasounds (Fig. 1). After resolution of his testicular nodule, cutaneous ENL and other HD complications, MTX was then gradually tapered and

successfully discontinued in July 2020. As of 2023, the patient has not presented recurrence of ENL episodes nor any other HD complication despite being off treatment. Furthermore, the right-sided testicular mass has remained non-palpable and asymptomatic clinically and stable on ultrasound examination.

Discussion

Testicular involvement is seen in 44–87 % of patients with LL, most commonly presenting as testicular atrophy, azoospermia, and hypogonadism [6,7]. The few described cases of testicular ENL have presented as generalized testicular tenderness and have been treated with MB-MDT, thalidomide, corticosteroids or orchiectomy in persistent cases; none have presented as intratesticular masses [7,8]. Intratesticular masses are managed by measurement of tumor markers and pertinent imaging studies. When malignancy is suspected, biopsy is rarely done to avoid seeding and a diagnostic orchiectomy is performed [8]. Rather than biopsy or orchiectomy, we provided a trial of immunosuppressive therapy with prednisone and MTX, shown to be an effective treatment for ENL [9]. This resulted in resolution of left intratesticular nodule, testicular pain, and a decrease in size of the non-palpable and asymptomatic contralateral mass. The patient’s presentation of left testicular tenderness with a palpable nodule, incidental right testicular nodule on imaging, and subsequent response to treatment favors intratesticular masses as an unusual presentation of ENL. Subcutaneous involvement of the polymorphonuclear lymphocytic

infiltrate in ENL may lead to replacement of adipocytes by fibrosis [10]. Thus, the remaining stable and asymptomatic right testicular nodule might represent post-inflammatory scarring or fibrosis. This case highlights the importance of a high index of suspicion in patients with LL and ENL who present with testicular nodules. Awareness of testicular involvement in this population is imperative to avoid life altering procedures such as orchiectomy.

Ethical approval

N/A

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Patient consent

Consent for the publication of all patient photographs and medical information was obtained.

CRediT authorship contribution statement

Adriana Figueroa-Diaz: Conceptualization, Writing – original draft, Writing – review & editing, Methodology, Visualization, Investigation. **Camila Cordero-Pacheco:** Writing – original draft, Writing – review & editing, Methodology, Visualization, Investigation. **Aida Quintero-Noriega:** Resources, Supervision, Investigation, Writing – original draft, Writing – review & editing, Funding acquisition.

Conflicts of interest

There are no conflicts of interest.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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